

REMARKS

Claims 1-11 and 13-22 are currently pending. Claims 1 and 11 are amended to more particularly point out and distinctly claim the subject matter for which patent protection is sought. Each of independent claims 1 and 11 are amended to recite that each of the one or more simultaneous responses to the sequences of spatially sparse stimuli are measured.

The following portions of the specification, at least, provide support for these amendments to claims 1 and 11:

Para	Text	Comments
[0004]	"in what might be called Multi-stimulus Evoked Responses (MSERs). The ability to record responses to concurrently presented stimuli to different component parts of the nervous system would clearly reduce some of the problems inherent in classic methods for recording evoked responses, in that the responses would represent the activity of component parts of the nervous system rather than the massed response of some or all the stimulated parts."	
[0008]	"simultaneously presenting two or more parts of the sensory system with respective sequences of stimuli,..." measuring one or more simultaneous responses by the subject to the sequences of stimuli, and determining weight functions from the responses".	A person skilled in the art would understand that the weight functions, such as those kernels, would be measured one for each sequences, each of which is applied to a different part of the nervous system, as for example in the cited patent 4,846,567 at [0005]. That relationship between individual responses (kernels) to the individual sequences is made clear later
[0009]	"The responses are generally linear or nonlinear functions of the stimuli and the weight functions may be Wiener or Volterra kernels."	
[0009]	"The temporally modulated stimuli should be sufficiently complex so as to permit estimation of some or all of the coefficients of linear and	

Para	Text	Comments
	non-linear weighting functions characterising <u>the measured responses to each stimulus presented to each part of the nervous system.</u> "	
[0021]	"(d) estimating some or all of the coefficients of the linear and non-linear weighting functions for <u>each stimulus sequence from the measured responses to said stimuli, to isolate separate responses from the separately and simultaneously stimulated component parts of the nervous system.</u> "	
[0032]	"Suitably, the temporally modulated stimuli and are sufficiently complex so as to permit estimation of some or all of the coefficients of linear and non-linear weighting functions <u>characterising the measured responses to each stimulus presented to each part of the nervous system.</u> "	
[0038]	"the stimuli having different sequences for each stimulated part that are spatially sparse across the non-time dimensions of the sensory dimensions stimulated"	
[0040]	"processing means for determining coefficients of linear and non-linear weighting functions for each stimulus sequence from the measured responses to said stimuli"	
Fig. 6	See Figure.	
[0053]	"FIG. 6 gives examples of responses to ensembles of stimulus sequences with there being one response per region such as shown in FIGS. 3 and 4"	
[0067]	"FIG. 6 gives examples of responses to each of the ensemble of independent stimulus sequences applied in a spatial layout like those of FIGS. 3 and 4. Polar angle corresponds to stimulus layout, eccentricity is linearized compared to actual stimulus, which was log-spaced. <u>There is thus one response waveform for each stimulus region.</u> "	

Claims 1-11 and 13-22 are currently pending. Claim 12 was previously cancelled. Independent claims 1 and 11 are amended in this response.

In relation to paragraph 1 of the Office Action, no response is required.

In relation to paragraph 2 to 13 of the Office Action, claims 1-5, 7-11, 13-17, and 19-22 have been rejected as being obvious under 35 USC §103(a) over Maddess *et al.* (US 2003/0163060) in view of Gevins *et al.* (US 2003/0013981).

Maddess *et al.* teaches that temporally sparse stimuli, brief stimuli delivered with longer aperiodic gaps (*i.e.*, null stimuli), where the mean rate of delivery of the transient stimuli is between 0.25 and 6 (or 25) stimuli per second per stimulus region provide larger responses with higher signal to noise ratios. This effect of temporally sparse stimuli is illustrated in Figure 7 of the instant patent application. Spatial sparseness refers to a few stimuli being presented across a space defined by non-temporal stimulus dimensions (see present application at [0015], [0036], [0077], [0099], and [0091]). The present application teaches that, surprisingly, even when stimuli of the same temporal sparseness are tested, those stimuli that are more spatially sparse increase signal to noise ratios further. This is best demonstrated by Figure 8 of the present application and the corresponding text associated with the drawing at paragraph [0104].

Maddess *et al.* and the present application indicate that the objective is to resolve the responses to presentations of the stimuli at each region in the ensemble defined by the non-temporal dimensions and that to achieve this appearance of stimuli at each location stimuli need to be modulated by aperiodic, that is, non-repeating, sequences. The sparse method is designed to measure the response to each of the ensemble of stimuli as shown at [0009], [0019], [0021], [0032], [0038], [0053], [0067], and [0008] in conjunction with [0086]. It is definitely not a method for measuring a pooled response of

the brain to the ensemble of stimuli as described at [0004]. More specifically Maddress *et al.* and the present application represent methods for increasing the size of the responses to each of the stimuli, not for decreasing the sizes of the responses. Also the specific examples of the present application permit several regions to be active at the same time on any given frame of the stimulus, that is, multiple stimuli may be delivered simultaneously, provided they are "relatively isolated spatially" (see the present application at paragraph [0077]).

Gevins *et al.* sets out a means of quantifying degeneration of cognitive function, the basic steps of which are:

1. Subjects performing repeated tests within a test session, where the tests involve the presentation of visual stimuli in a cognitive or memory related task.

2. Recording: a) cognitive performance behaviorally, and b) brain responses preferably by EEG. Also preferably the same tests are repeated at a later date. Some of the repeated tasks can be more difficult versions, but all tasks are to be repeated.

3. These records should be made with various treatments such as drugs, sleep deprivation or sensory deprivation. Alternatively the treatments may instead be severities of disease exposure.

4. The brain responses measured by an EEG are gross pooled measures that in no way measure the response to each stimulus as described at [0116], [0117], [0122], [0123], [0124], [0129], [0135] to [0138] of Gevins *et al.* No attempt is made and no benefit is indicated for measuring the responses to the individual stimuli. The stimuli or lack of stimuli are only provided as a means to stress the working memory of a subject.

5. Instead of measuring responses to individual stimuli *Gevins et al.* measure the effects of the treatments while the cognitive task is performed. *Gevins et al.* do not seek to produce stimuli which increase the size or reliability of the responses to the stimuli. *Gevins et al.* only examine changes in EEG brain responses produced by the treatments, not the stimuli.

6. *Gevins et al.* teach that the optimal changes brain response to the treatments, not the stimuli, may be either increases or decreases of brain activity as shown at [0123], [0124], [0129], [0132], [0136], [0137], [0138], [0156], [0169], [0179], [0180], [0192], [0211], [0225] of *Gevins et al.* This is best shown for Experiment 1 in Table 1 at paragraph [0124] of *Gevins et al.* Clearly if decreases in response can be optimal, as *Gevins et al.* teach, that would be the opposite of what the present application teaches.

Gevins et al. use several different cognitive tasks while the responses to various treatments are assessed. The treatments used in the 9 experiments of *Gevins et al.* are described in [0103], [0153], [0165], [0173], [0204], [0220], and [0237] of *Gevins et al.* The fact that more than one task is used in *Gevins et al.* indicates that *Gevins et al.* do not place particular value any given task. Perhaps the most commonly employed task in *Gevins et al.* is that of Experiment 1. It is often difficult to judge whether it is used for the other experiments, but it is certainly not used in Experiments 7 and 8. Overall *Gevins et al.* are not at pains to explain what task they used. The task of Experiments 1 is not mentioned in any of the claims of *Gevins et al.* and is never mentioned as being optimal in increasing response sizes. Apparently *Gevins et al.* have very little regard for the value of that task.

The task of Experiment 1 presents a single letter at one of many locations on a display. The position of the letters varies randomly over time: see *Gevins et al.* at paragraph [0112]. The subjects have to perform a working memory task while watching the stimuli. Importantly, no mechanism is provided to insure that from presentation to presentation that near neighbour regions are not stimulated. In particular no mechanism is provided for insuring that the stimuli remain spatially sparse even when they are being delivered at the rate of tens or hundreds per second as in the present application (see below). Thus, spatially *Gevins et al.* does not teach or even suggest the method of the claimed invention. The combination of *Maddess et al.* and *Gevins et al.* does not suggest or teach this aspect.

Although in Experiment 1 of *Gevins et al.* the letters are delivered randomly, the letters are delivered only one at a time. Responses to the individual stimuli are not recorded, with only one stimulus being presented every 4.5 s, to measure the evoked EGG response to each stimulus, and average them for particular locations, or for particular hits or misses by the subject. By contrast in the claimed invention, separate responses to each of the stimuli are recorded. So *Gevins et al.* does not place any value on recording responses to the individual stimuli. Instead, the average power in standard frequencies bands, alpha, delta, theta in response to large numbers of the stimuli are recorded: see *Gevins et al.* at paragraph [0116] "average power was extracted from individual spectral bands at individual electrode sites". Thus, in no sense are the responses to the individual stimuli recorded or estimated in any way. Only the differences in the average EEG responses to the different treatments were recorded.

It is submitted that there is no basis for combining Maddess *et al.* and Gevins *et al.*, as set out below:

1. The task of Gevins *et al.* are delivered one at a time every 4.5 s (see Gevins *et al.* at paragraph [0112]). In Maddess *et al.*, the slowest stimulus was at 4 s per region, and there were 8 regions, so the stimuli came 8 times that rate in aggregate, that is, at 2 per second and so several stimuli could appear at once on the display. At the highest optimal rate of Maddess *et al.*, there would be $6 \times 8 = 24$ stimuli per s on the display. Hence, the appearance of the stimuli would be very different from those in Gevins *et al.* The presence of multiple stimuli on the display is shown in Figures 3 and 4 of the present application. In the present application, there were 56 stimulus regions. Even at the slowest rate at which the benefits of spatial sparseness were demonstrated, 4.2 stimuli/region/s, the stimuli were arriving at $4.2 \times 56 = 235.2$ /s on the display, that is, nothing like the 1000 times slower stimulus of Gevins *et al.*

2. In both Maddess *et al.* and Gevins *et al.*, there is also no restriction on whether a subsequent stimulus should appear near a previous stimulus. The restriction of the appearance of near neighbours is the key feature of spatially sparse stimuli as illustrated in Figure 3, 11, 12, 13 and the associated text of the present application. The Office Action accepts this difference between Maddess *et al.* and the present application, and so the same should be accepted for Gevins *et al.* Hence, the stimuli of Gevins *et al.* do not possess this essential feature of spatially sparse stimuli.

3. No recordings of responses to the individual stimuli are made in Gevins *et al.*, only pooled responses to many stimuli (see [0116], [0117], [0122], [0123], [0124], [0129], and [0135] to [0138] where the only recorded discrimination is between the

treatments, not stimuli). Thus only the average effect of treatment is recorded, not the effect of individual stimuli. Gevins *et al.* mention no desire to record anything about the responses to individual stimuli anywhere.

4. Rather than responses to individual stimuli the optimal pooled responses averaged for each treatment are frequently decreases (reductions) in response rather than increases (see Gevins *et al.* at paragraphs [0123], [0124], [0129], [0132], [0136], [0137], [0138], [0156], [0169], [0179], [0180], [0192], [0211], and [0225]). So if there were any influence of the stimulus it was frequently to reduce response size, not increase it as in the present application.

5. To record the responses to the individual stimuli each region in Maddess *et al.* needs to be modulated by a separate pseudo-random sequence. In Gevins *et al.*, a single sequence is used to drive presentations at all regions.

6. It is a necessary feature of the present application that no stimulus ever repeats. The stimuli are random sequences. In Gevins *et al.*, blocks of stimuli are repeated. The text of Gevins *et al.* at [0265] states that this repetition would be optimal. Again, non-repeating and repeating stimuli would provide a very different sensory experience to the subjects.

Thus, Maddess *et al.* teaches no value in restricting new stimuli to appear away from previous stimuli in space (*i.e.*, non-temporal stimulus dimensions). Stimulus presentation location in space is random. Similarly, Gevins *et al.* teach no value in restricting new stimuli to appear away from previous stimuli in space, because as in Maddess *et al.* stimuli appear randomly at any location. Maddess *et al.* and Gevins *et al.*, separately and in combination, do not suggest restricting the presence of near

spatial neighbours. In the event that temporally sparse sequence can be somewhat spatially sparse, this chance degree of sparseness is not sufficient to produce the improved signal to noise ratio of the present application, which insures spatial sparseness (*e.g.*, see Figs. 3 and 10 to 13).

Furthermore, *Gevins et al.* do not record response to the individual stimuli and provides no such means. *Gevins et al.* teaches that it is optimal to ignore responses to individual stimuli and instead pool responses to all stimuli. This teaches away from *Maddess et al.* and the present application. In *Gevins et al.*, response decreases are frequently said to be optimal, also the opposite of *Maddess et al.* and the present invention.

Gevins et al. also teach that stimuli presented one at a time at a very slow aggregate rate (up to 1000 times slower) are optimal. Again, this teaches away from the present application. The stimuli of the present application and *Gevins et al.* are not of similar appearance.

Finally, *Gevins et al.* teach that repeating stimuli are optimal. This also teaches away from the present application.

It is therefore submitted that *Maddess et al.* and *Gevins et al.*, alone or in combination, do not teach or even suggest the claimed invention defined by independent method claim 1. Thus, claim 1 is in condition for allowance. Likewise, claims 2-10 being dependent claims of an allowable base claim are themselves in condition for allowance.

It is submitted that *Maddess et al.* and *Gevins et al.*, alone or in combination, do not teach or even suggest the claimed invention defined by independent apparatus

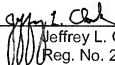
claim 11. Apparatus claim 11 tracks on method claim 1. Thus, for the reasons submitted above in respect of claim 1, claim 11 is also in condition for allowance. Likewise, claims 13-22 being dependent claims of an allowable base claim are themselves in condition for allowance.

In relation to paragraphs 16 and 17 of the Office Action, no further comment is required.

In view of the above, all of pending claims 1-11 and 13-22 are submitted to be in condition for allowance. Early notification to that effect is respectfully requested.

Respectfully submitted,

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October 23, 2009

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